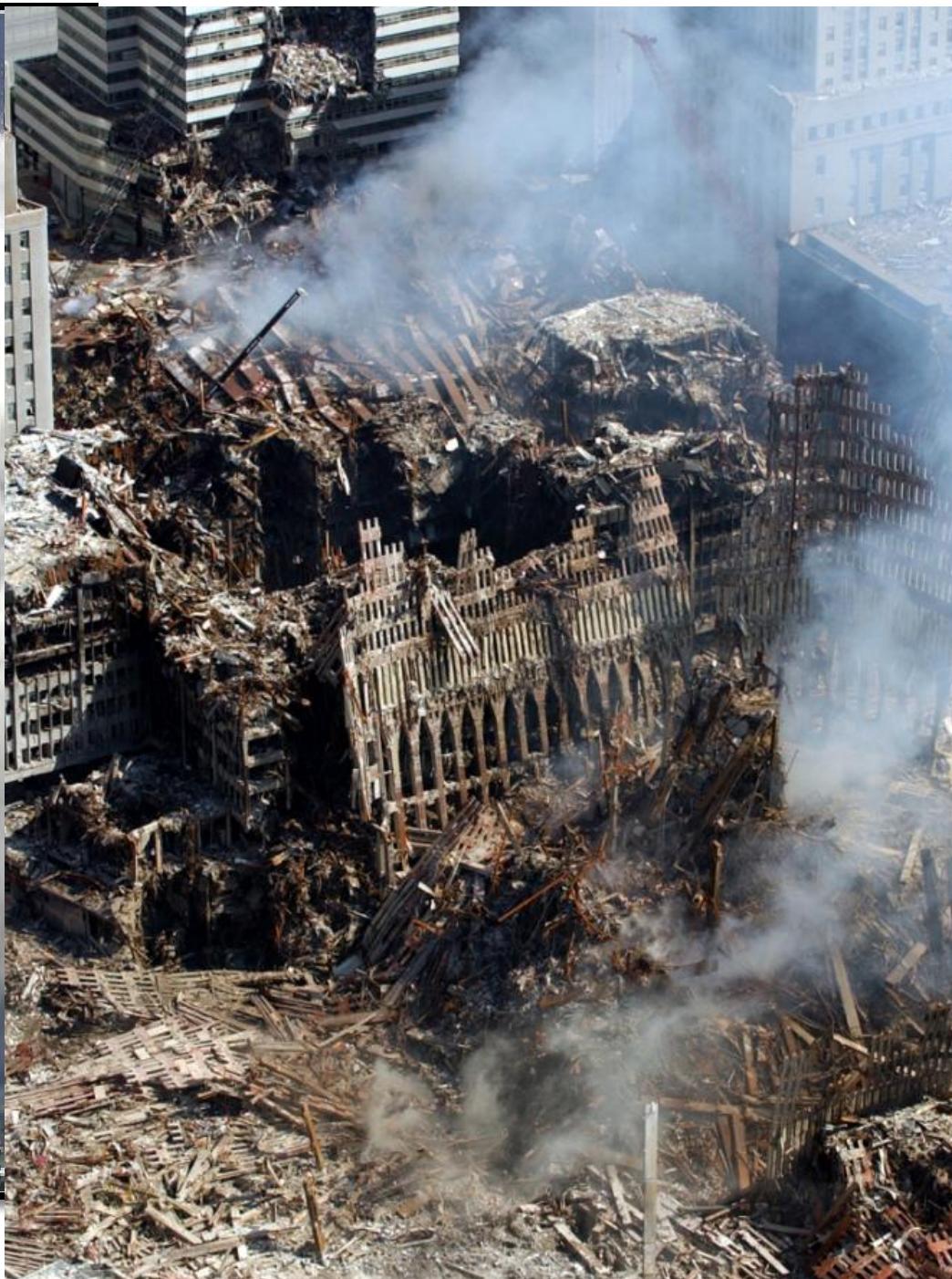


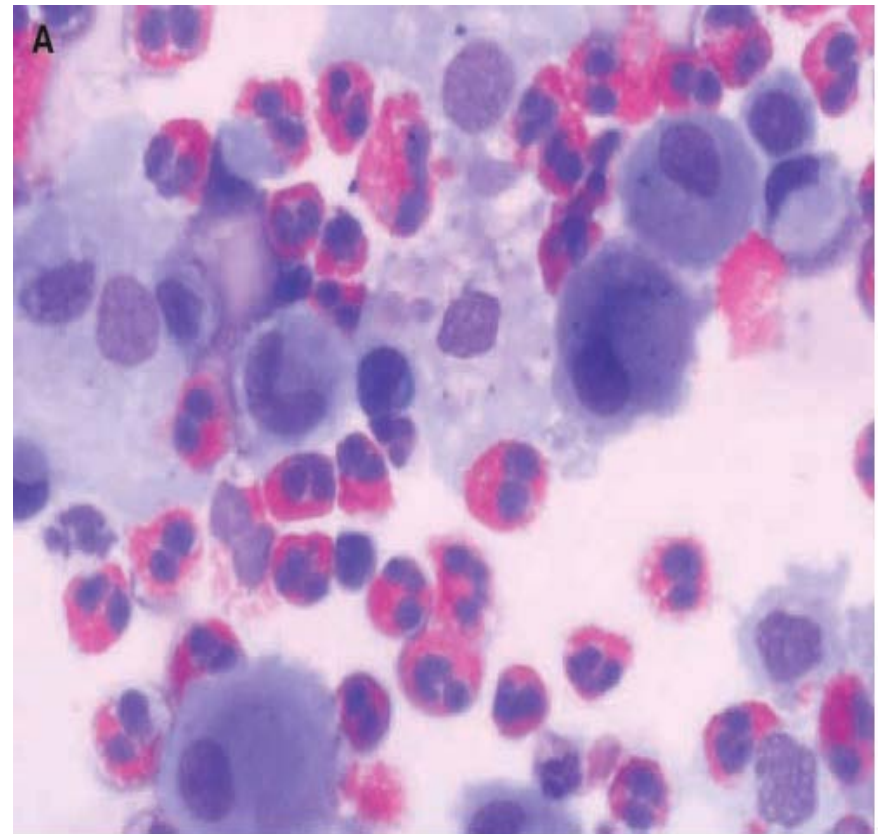


What we now know about the WTC dust particles

- Particle quantity and size
 - 1.2 million tons of building materials
 - 90% particles $>10\ \mu\text{m}$ diameter
 - 11,000 tons of particles $< 2.5\ \text{mm}$ were released
 - Gases and fumes from fires that burned until December 19, 2001

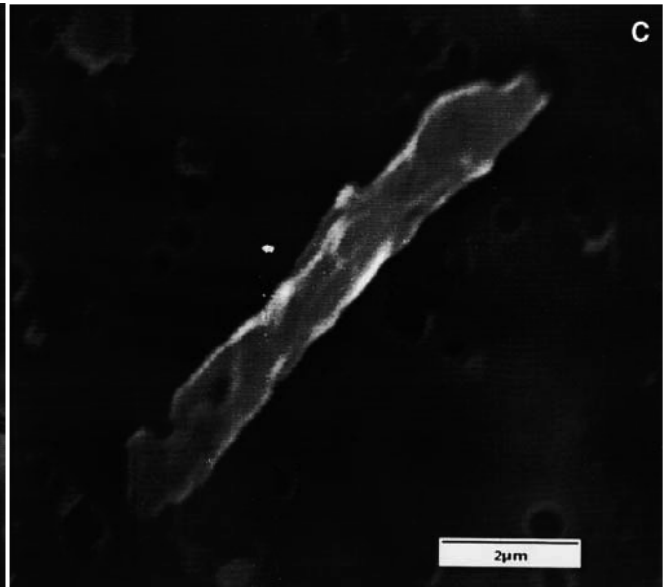
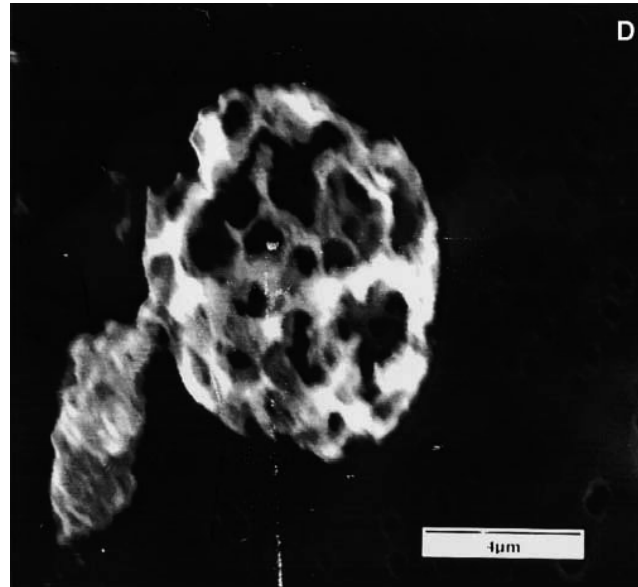
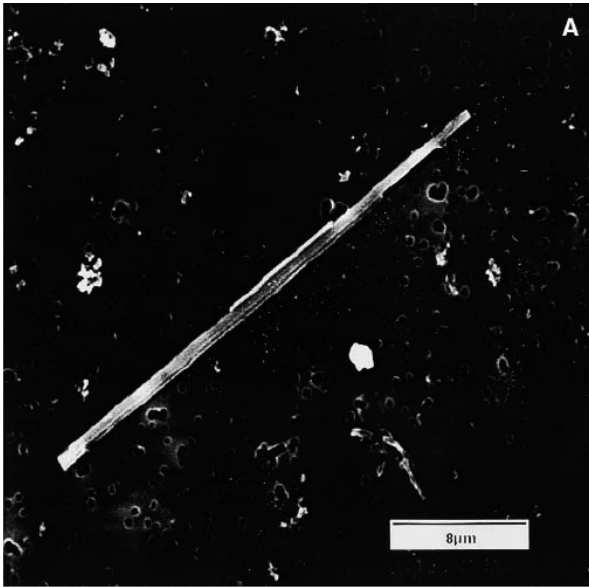


Early onset disease: Acute eosinophilic pneumonia in a firefighter





Mineralogic analysis of bronchoalveolar lavage from firefighter



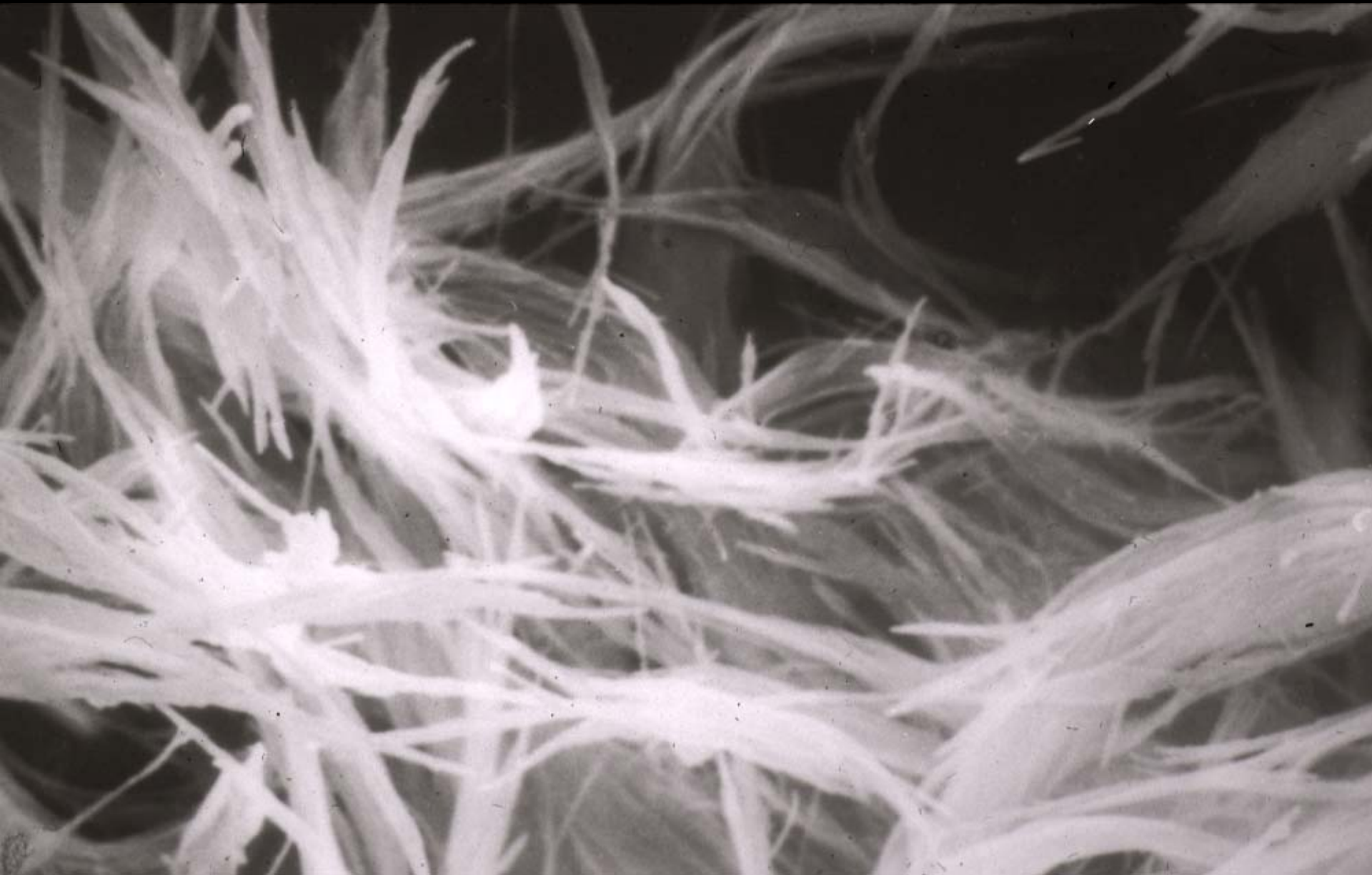
(A) Amosite asbestos fiber (uncoated)

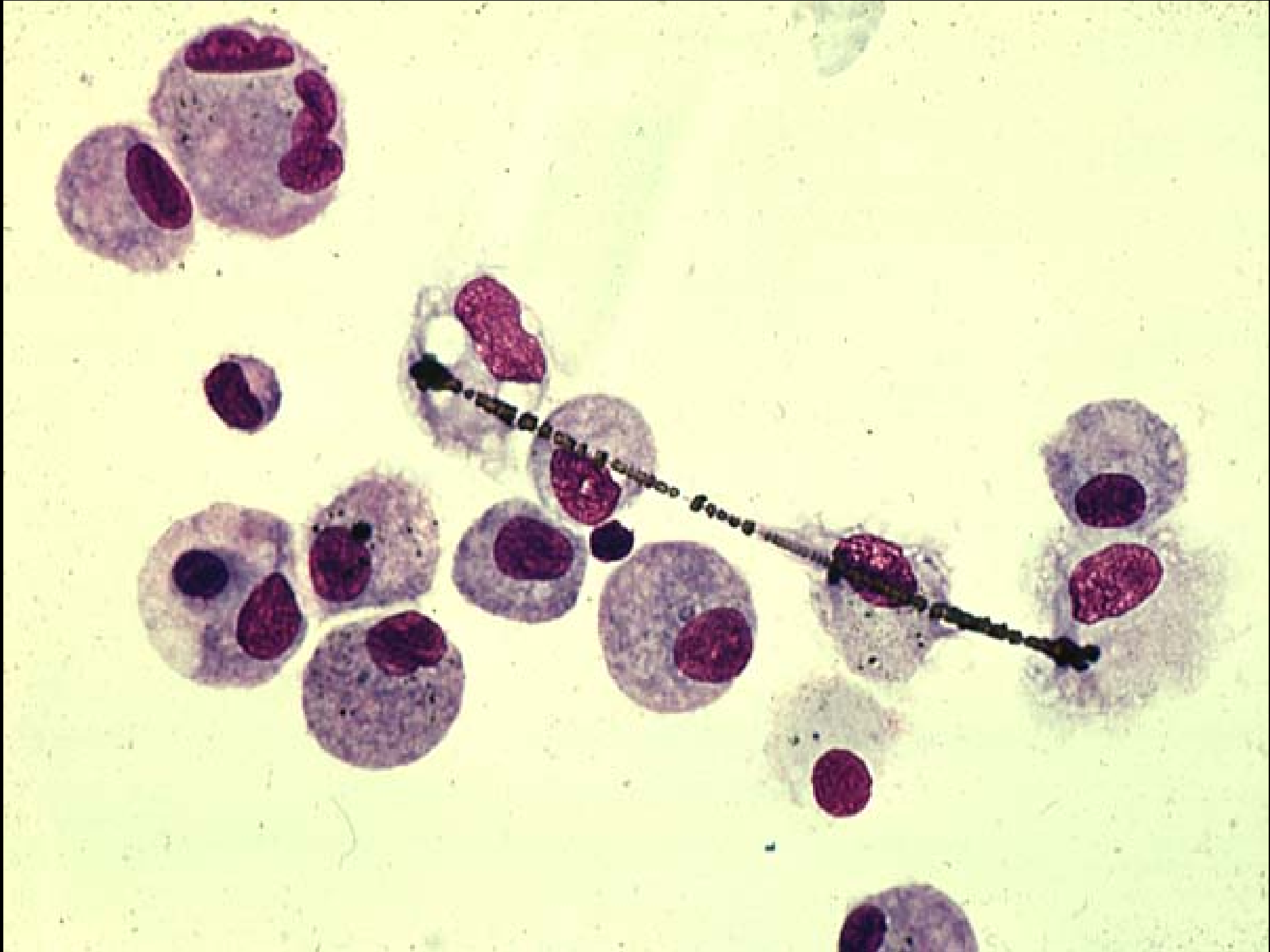
(B) Fly ash particle

(C) Degraded fibrous glass.

305 commercial asbestos fibers/ 10^6 macrophages

Chrysotile Asbestos



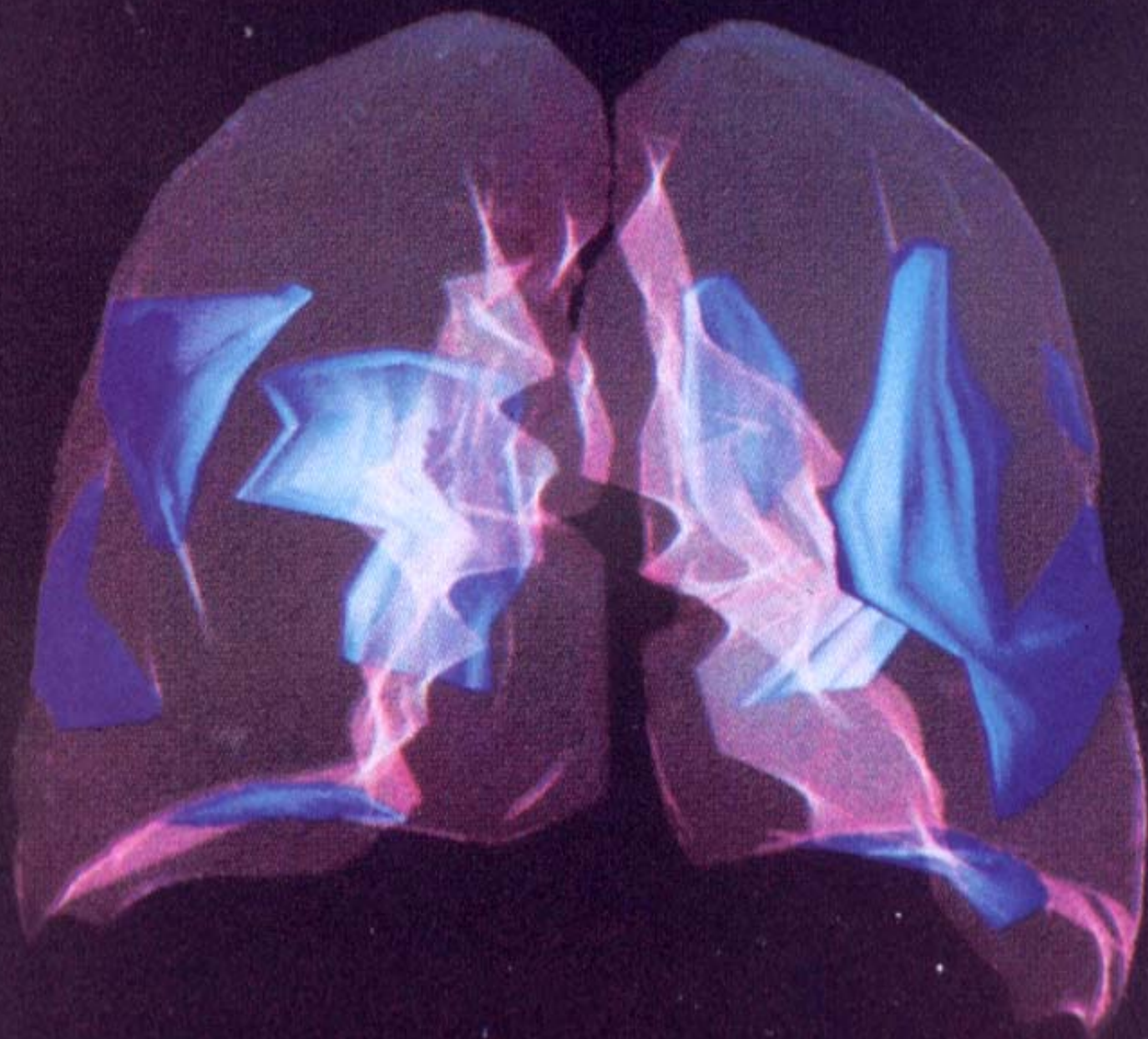


LUNG CANCER AND ASBESTOS EXPOSURE

- North American insulators union with 17,800 workers followed from 1967-1987 revealed
 - ▶ Lung cancer 1166 deaths 267 expected RR 4.4
 - ▶ Mesothelioma 457 deaths (9%)
 - Synergism with cigarette smoking
 - ▶ Risk decreases dramatically after quitting
 - Since the removal of asbestos from insulation materials in the early 1970's, death rates have declined for lung cancer but continued to increase for mesothelioma
-

Mesothelioma

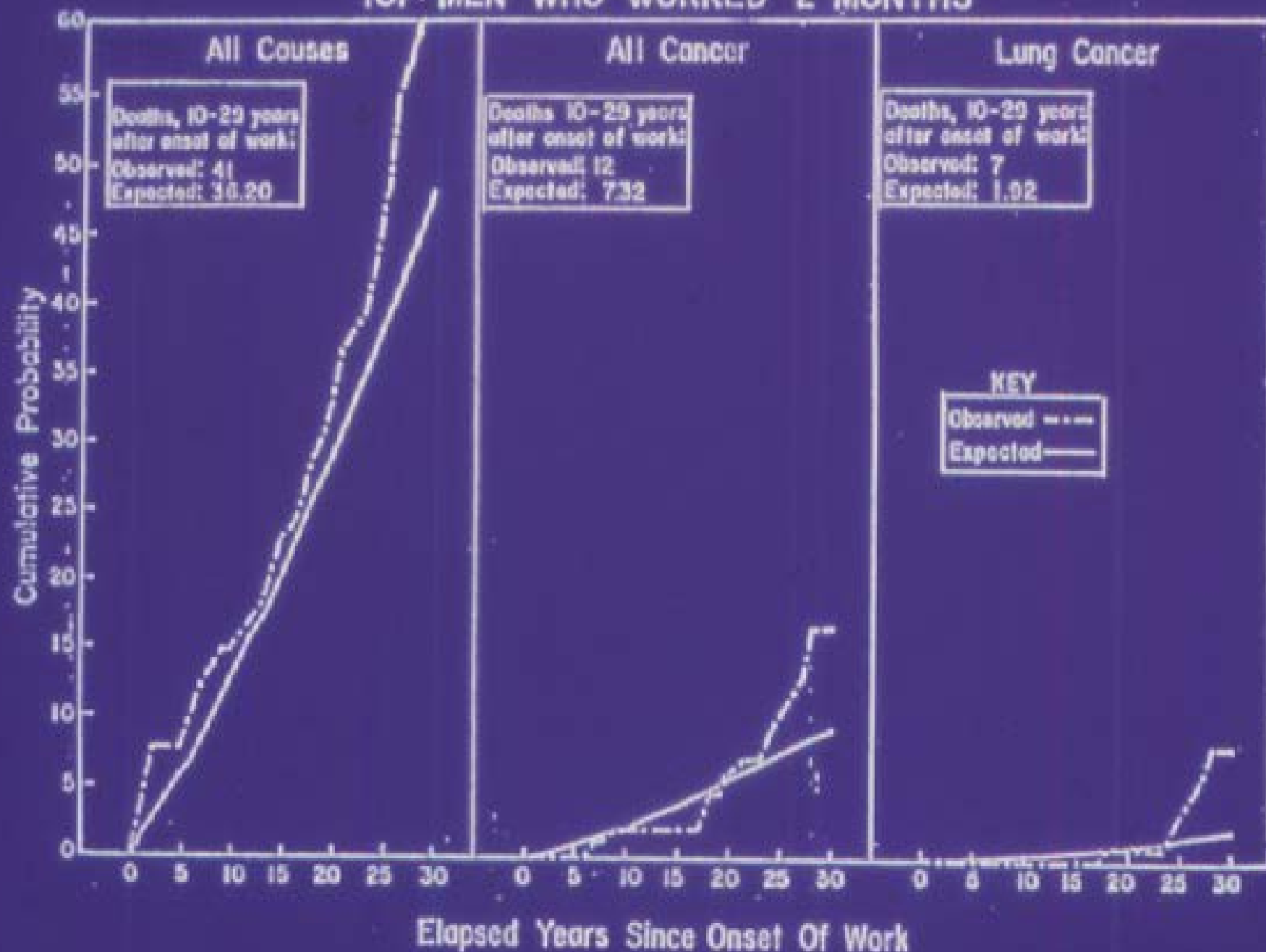




PLEURAL PLAQUES AND RISK FOR BRONCHIAL CARCINOMA AND MESOTHELIOMA

- Epidemiologic survey of 1,596 men with pleural plaques in Uppsala, Sweden, were followed from 1963-1985.
 - Bilateral lesions
 - ≥ 5 MM thick and/or calcified, well-demarcated.
 - No remnants of pleurisy, i.e. costophrenic angles not obliterated.
- 50 Bronchial carcinomas observed while 32.1 expected after correction for smoking (O/E 1.6; CI 1.2-2.1).
 - 2.3 (CI 1.1-4.4) with asbestosis
 - 1.4 (CI 1.0-2.0) without asbestosis
- 9 Mesotheliomas with 0.8 expected (O/E 11.3; CI 5.1-21.4).

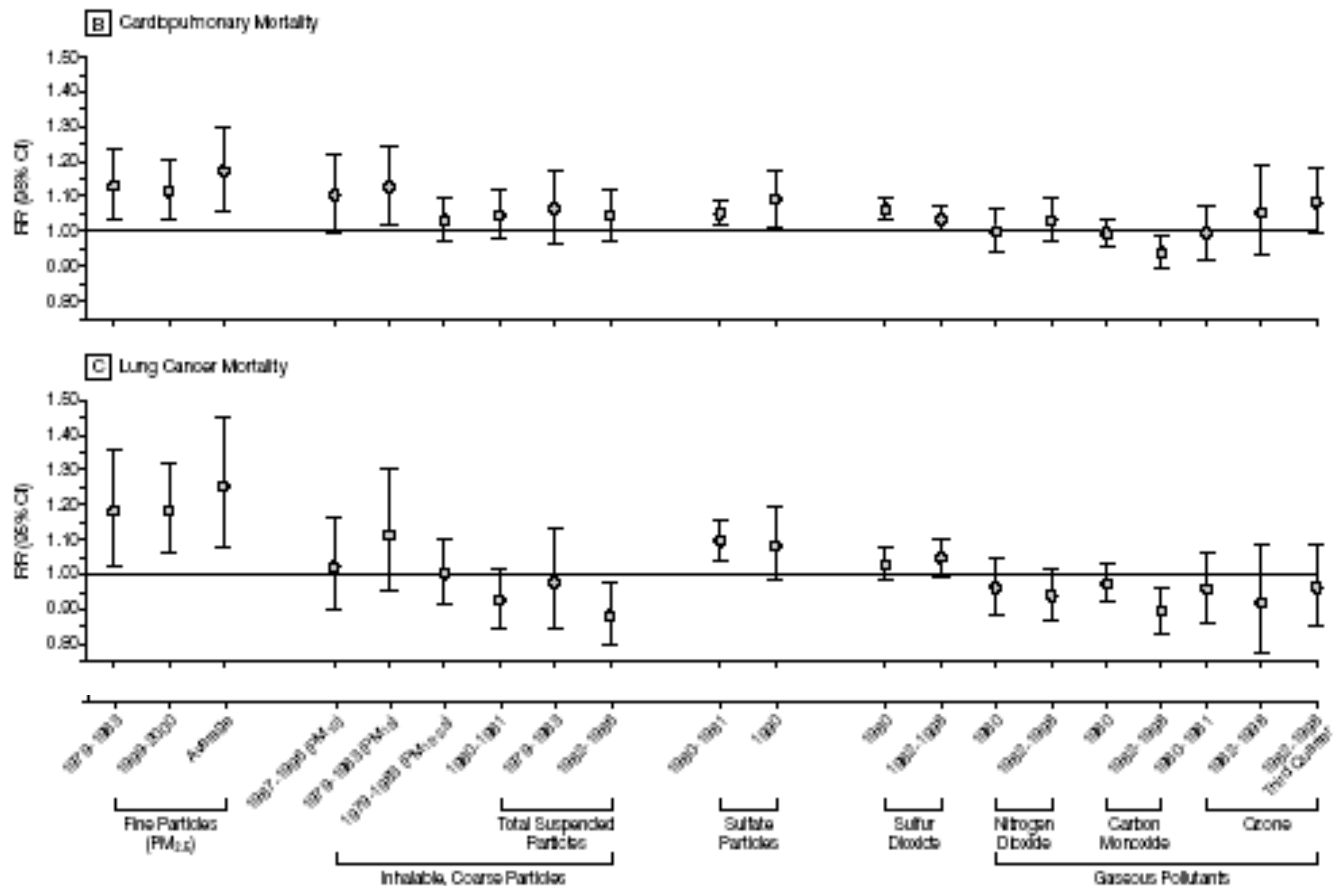
101 MEN WHO WORKED 2 MONTHS



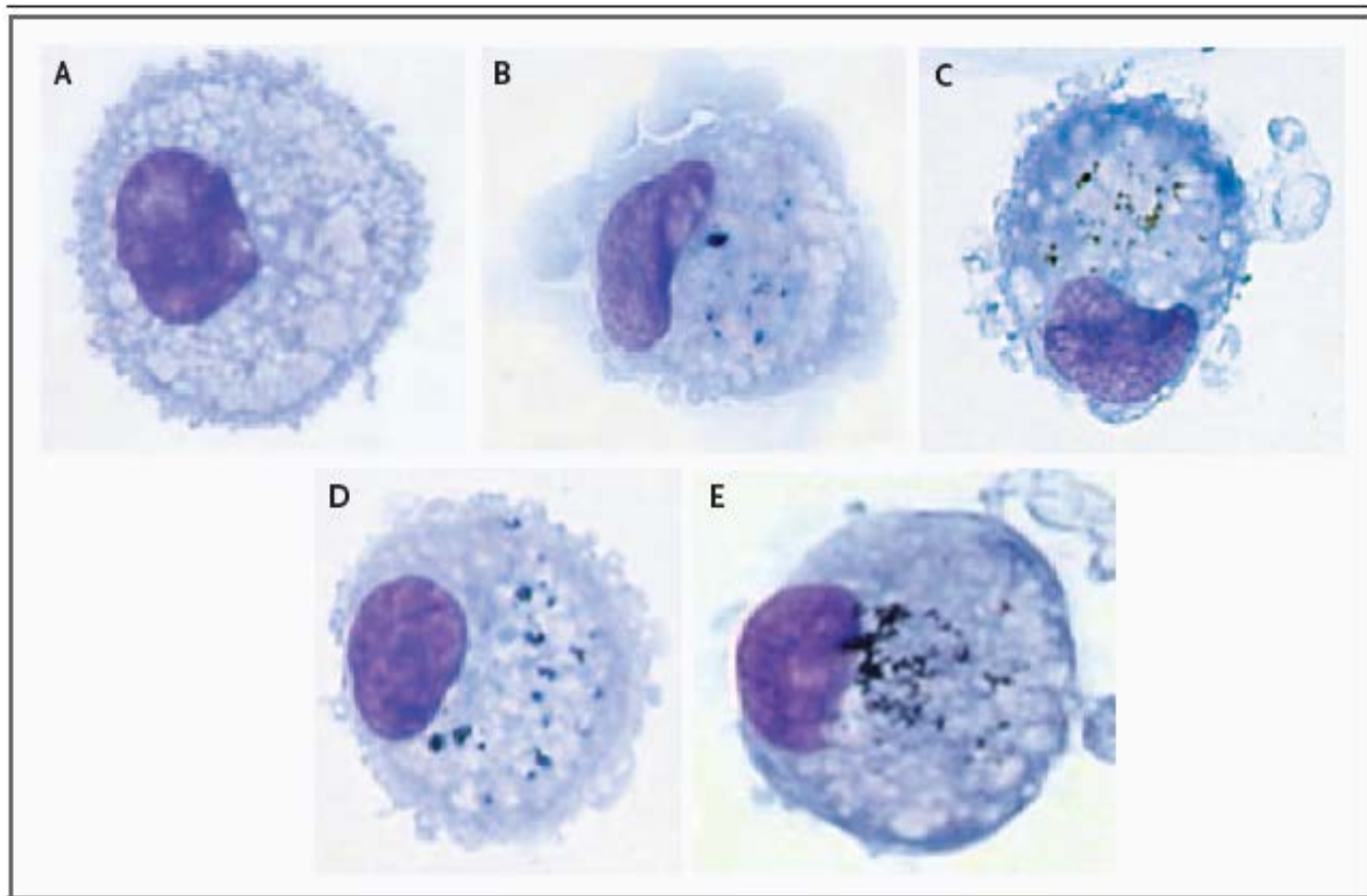
American Cancer Society Follow-up for Long Term Health Effects

- ACS enrolled 1.2M adults in 1982 and a questionnaire assessed age, sex, race, weight, smoking, education, diet, alcohol, and occupation.
- 500K adults were linked with air pollution data for metropolitan areas throughout the U.S. with vital status and cause of death data through December 31, 1998.
- $PM_{2.5}$ and SO_2 were associated with all-cause, cardiopulmonary, and lung cancer mortality.
- Each $10\mu g/m^3$ elevation in $PM_{2.5}$ was associated with approximately 4%, 6%, and 8% increased risk of all-cause, cardiopulmonary, and lung cancer mortality, respectively.
- Coarse fraction $PM_{10-2.5}$ not consistently associated with mortality.
- JAMA 2005; 287: 1132-41.

Adjusted Mortality Relative Risk (RR) Evaluated at Subject-Weighted Mean Concentrations



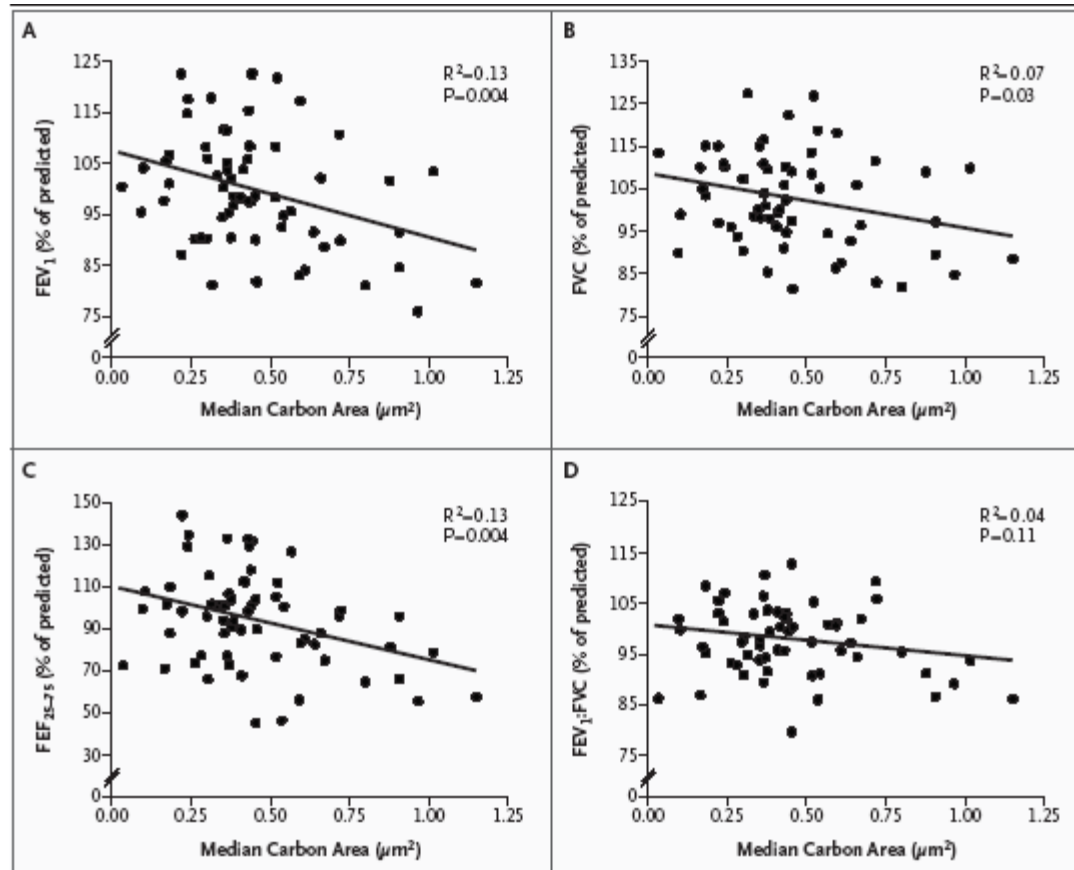
Representative Images of Carbon in Airway Macrophages from Healthy Children



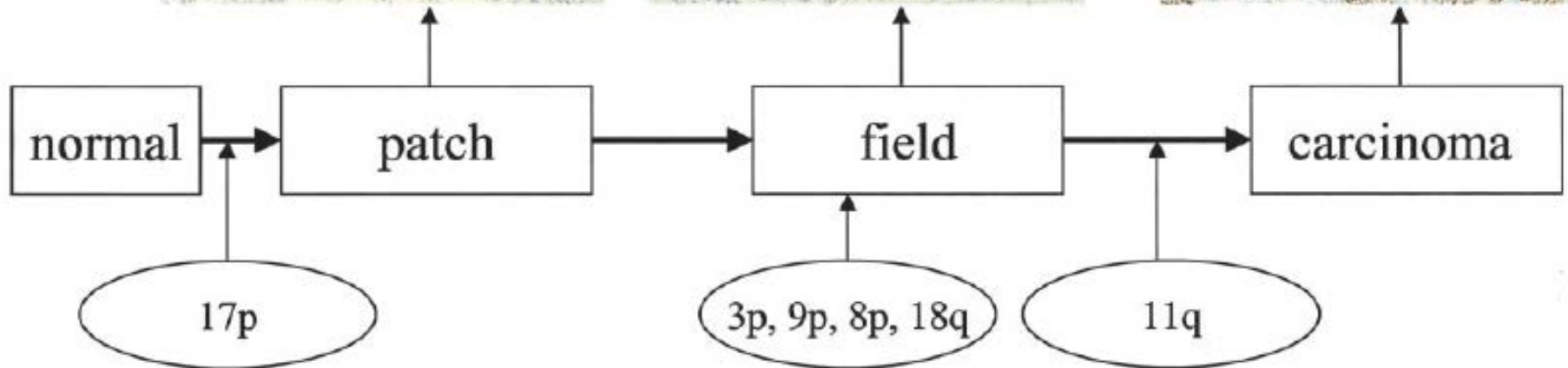
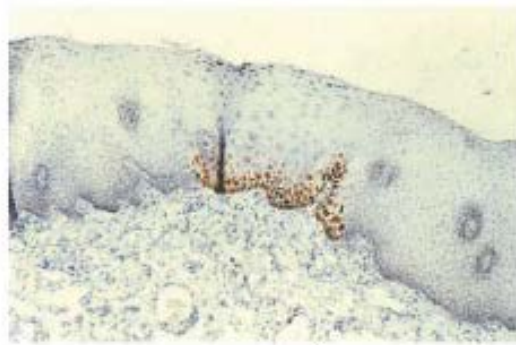
Carbon in Airway Macrophages and Lung Function in Children

- Alveolar Macrophages (AMs) reflect a particle burden from occupational/environmental exposure.
- Children aged 8-15 U.K. (excluding parental smoking, house with coal combustion) 64 healthy children, 9 with asthma enrolled. Salivary cotinine measured.
- PM₁₀ recorded including hourly near traffic plus annual; PFT; induced sputum with C area calculated under light microscopy.
- Each increase in 1.0 μm^2 in C associated with 17% decrease in FEV₁ % predicted and 12.9% in FVC % predicted; Each increase in 1.0 $\mu\text{g}/\text{m}^3$ PM₁₀ was associated with a 0.115 μm^2 in C.
- Increased primary PM₁₀ was inversely associated with FEV % predicted.
- NEJM 2006; 355: 21-30.

Associations between Carbon in Airway Macrophages and Lung Function in Healthy Children



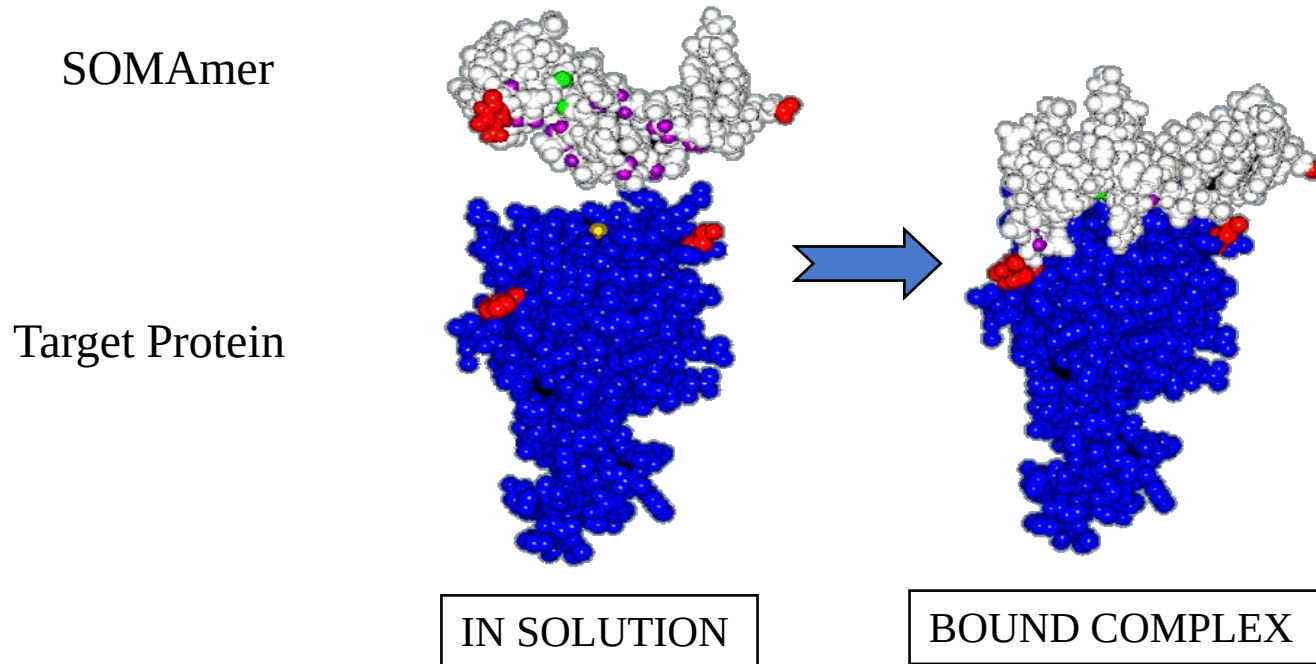
Field Cancerization of Squamous Cell Carcinoma of the Lung



Cancer Res 2003; 63: 1727.

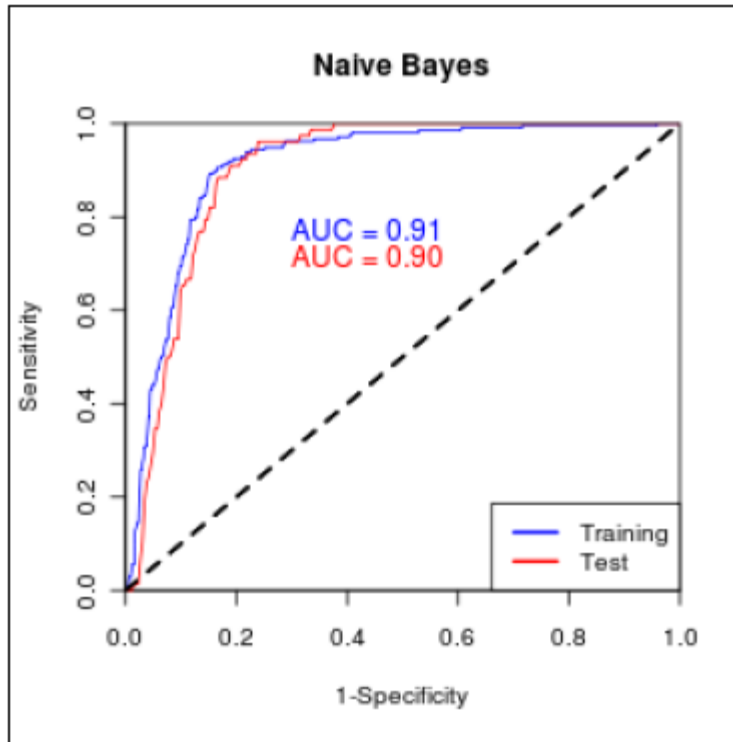
SOMAmers: Unique DNA Reagents for Protein Detection

Red, green, purple atoms are modified nucleotides that provide binding energy



- Single-stranded nucleic acids that bind with high affinity and specificity-currently available SOMAmers (1,043).
- The limits of detection average (300 fM) and the overall dynamic range spans 7 logs using different dilutions with a ~6% coefficient of variation.
- PLoS ONE 2010; 5(12): e15003. (December 2010)

SomaLogic



89% sensitivity and 83% specificity.

Biomarker	UniProt ID	Direction*	Description
Cadherin-1	P12830	down	cell adhesion, transcription regulation
CD30 Ligand	P32971	up	cytokine
Endostatin	P39060	up	inhibition of angiogenesis
HSP 90 α	P07900	up	chaperone
LRIG3	Q6UXM1	down	protein binding, tumor suppressor
MIP-4	P55774	up	monokine
Pleiotrophin	P21246	up	growth factor
PRKCI	P41743	up	serine/threonine protein kinase, oncogene
RGM-C	Q6ZVN8	down	iron metabolism
SCF sR	P10721	down	decoy receptor
sL-Selectin	P14151	down	cell adhesion
YES	P07947	up	tyrosine kinase, oncogene